Open Access
J. Glob. Innov. Agric. Sci., 2023,11(4):455-480.
ISSN (Online): 2788-4546; ISSN (Print):2788-4538
DOI: https://doi.org/10.22194/JGIAS/23.1234
http://www.jgiass.com

Mycotoxin production by *Fusarium* species and a recent deep insight into management through biocontrol approaches

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Fusarium infection has become a significant and widespread concern in modern agriculture, posing a substantial threat to numerous essential crop plants. The pernicious fungal pathogen has been causing widespread destruction in diverse areas, resulting in severe consequences for both food security and economic stability. Mycotoxins, which are secondary metabolites produced by a wide variety of fungi, present serious risks to the health of both humans and animals and have the potential to result in considerable financial losses for the agricultural and food industries. The genus *Fusarium* is particularly infamous for its capacity to produce a diverse range of mycotoxins. The present summarized study highlights the recent progression of *fusarium* infection towards various pivotal agricultural crop plants with their life cycle, morphological and microscopic characteristics, and pathogenicity factors. *Fusarium* species are well-known for their ability to produce mycotoxins, such as zearalenones, fumonisins, Trichothecenes, Deoxynivalenol, Nivalenol, and T-2 toxins which are detrimental secondary metabolites that contaminate a wide range of agricultural products, with a particular emphasis on grains and cereals. The new emerging mycotoxins are producing new challenges for their control and serious risks to human health. The identification of *Fusarium* mycotoxins and the implementation of efficient biocontrol strategies to detoxify the mycotoxins through Trichoderma, Plant Secondary Metabolites, Lactic Acid Bacteria, Edible Mushrooms, and various Enzymes are essential measures for guaranteeing food safety and protecting public health. The mentioned biocontrol approaches to detoxify the mycotoxins are also discussed and addressed.

Keywords: *Fusarium* mycotoxins, pathogenicity factors, trichothecenes, biocontrol agents, enzymatic detoxification.

INTRODUCTION

Fusarium is an important genus of imperfect fungi that contains 20 different species of destructive phytopathogenic filamentous fungi, 14 of which are pathogenic to plants. Among these, the most significant plant pathogenic species are *Fusarium oxysporum*, *Fusarium solani*, and *Fusarium chlamydosporum*. These species are found everywhere, from tropical to temperate areas of the world and even in harsh climates (Rehman *et al.*, 2023; Shabeer *et al.*, 2021). They have a wide host plant range and cause significant economic losses in all cereal crops in Western Europe (WE) and North America (NA), including rice plants in Thailand, Japan, and Taiwan, wheat, cotton, and barley in China, and in other countries, causing devastating impacts on timber trees in the forest (Suga and Hyakumachi, 2004). *Fusarium* species are associated swith the production of different kinds of secondary metabolites, such as gibberellin and zearalenone, which are the most significant plant growth regulators and are also used to accelerate the growth of animals (Nesic and Nesic, 2013; Qiu *et al.*, 2020). Trichothecenes and fumonisins produced by these species are also pathogenic to humans and animals and can cause mycotoxicosis when they are fed contaminated food (Hao *et al.*, 2022; Li *et al.*, 2020). *Fusarium* spp. can survive on dead and decaying plant material, can sustain itself in soil for up to 16 years in the absence of a host, and also acts as an important biodegrading agent (Early 2009).

Ali, A., F. Ölmez, M. Tatar, I. Tabbasum, H. Azeem, R. Sarwar and F. Ali. 2023. Mycotoxin production by *Fusarium* species and a recent deep insight into management through biocontrol approaches. Journal of Global Innovations in Agricultural Sciences11:455-480.
[Received 17Oct 2023; Accepted 28 Nov 2023;Published 22 Dec 2023]

Mycotoxins are the toxic secondary metabolites produced by all species of the genus *Fusarium*. They cause virulence during the development of infections in host plants and are also responsible for severe health problems in humans and animals (Table 1) that consume contaminated grains (Penagos-Tabares *et al.*, 2021). Depending on the type and concentration, different types of symptoms are thought to be produced by different kinds of mycotoxins (Cinar and Onbaşı, 2019; Lindemann *et al.*, 2022). Fumonisins, zearalenone, and trichothecenes are the mycotoxins that are produced by different species of *Fusarium*, including *F. solani*, *F. subglutinans, F. sporotrichioides, F. crookwellense, F. poae, F. venenatu, F. scirpi, F. chlamydosporium, F. semitectum, Fusarium avenaceum, F. graminearum, F. nygamai, Fusarium camptoceras, F. tricinctum, F. culmorum, F. proliferatum, F. equesiti, F. oxysporum, F. nivale, F. sambucinum, F. tumidum, F. compactum, F. moniliforme, and Fusarium acuminatum* (Del-Palacio *et al.*, 2023; Ekwomadu and Mwanza, 2021; Elkenany and Awad, 2021; Garcia-Cela *et al.*, 2022; Huang *et al.*, 2019; Perincherry *et al.*, 2019; Twarużek *et al.*, 2021).

Zearalenone is a type of mycotoxin produced by *F. graminearum* and certain related species of *Fusarium* sambucinum. However, it is important to note that these mycotoxins are not known to be associated with any diseases specifically affecting wheat. Zearalenone has been identified as a potentially advantageous mycotoxin due to its application in promoting the growth of cattle (Yu *et al.*, 2004). Fumonisins are associated with the ear rot of corn (not involved in disease) and excreted by *F. moniliforme*, *F. verticilloides*, *F. nygamai*, *F. proliferatum*, and *F. napiforme* (Desjardins and Plattner, 2000; Keller and Sullivan, 1996; Nelson *et al.*, 1992). They are carcinogenic in nature, exert harmful effects on the health of humans and animals, and also badly affect the liver as well as the kidney. Some fungal species related to *F. sambucinum* and *F. graminearum* are involved in the production of zearalenone (Nahle and Atoui, 2021). These are the beneficial toxic substances that can be used to enhance the growth of animals and are also associated with the diseases of wheat.

The detoxification of mycotoxins, which are synthesized by various fungal species, can be achieved through the use of

Table 1. A list of mycotoxins produced by different species of *Fusarium* and their impacts are summarized.

Sr.	Name of mycotoxin	Compound of mycotoxin	Mycotoxin-producing sp.	Effect of mycotoxin	References
1	Trichothe-cenes	Diacetoxyscirpenol, Deoxynivalenol, T-2 toxin, HT-2 toxin, Nivalenol	*F. camptoceras, F. nivale, F. venenatu, F. acuminatum, F. moniliforme, F. scirpi, F. oxysporum, F. tumidum, F. avenaceum, F. poae, F. sambucinum, F. graminearum, F. proliferatum, F. chlamydosporium, F. nygamai, F. subglutinans, F. compactum, F. crookwellens, F. solani, F. semitectum, F. tricinctum, F. equesiti, F. culmorum*, and *F. sporotrichioides*	Trichothecenes can irritate the gastrointestinal tract, causing nausea, vomiting, stomach discomfort, and diarrhea, impair the immune system, affect blood cells and coagulation, and cause redness, itching, and inflammation.	(Desjardins and Plattner, 2000; Mulè *et al.* 1997; Pitt *et al.*, 2000)
2	Fumonisins	Fumonisins B1, B2 and B3	*F. nygamai, F. verticillioides, F. napiforme, F. dlamini* and *F. proliferatum*	Pulmonary edema, hepatotoxicity, leukoencephalomalacia and cancer	(Desjardins 2006; Marin *et al.*, 2013)
3	Zearalenone	-	*F. incarnatum, F. cerealis F. gramineraum, F. culmorum, F. verticillioides* and *F. equiseti*	Estrogenic syndromes in swine boost cattle growth	(Desjardins 2006; Marin *et al.*, 2013; Pusateri and Kenison, 1993)
4	Deoxynivalenol	-	*F. culmorum* and *F. graminearum*	Astrointestinal toxicity, inflammation of the central nervous system	(He *et al.*, 2018)
5	Enniatins and Beauvercin	-	*F. avenaceum, F. trincinctum, F. verticilliode F. langsethiae, F. subglutinans, F. sambucinum, F. sporotrichioides F. sporotrichioides*, and *F. proliferatum*	No effects	(Desjardins 2006; Logrieco *et al.*, 1998)
6	Butenolide	-	*F. graminearum*	Butenolide brings on Fescue foot in cows and poisoning in mice	(Desjardins 2006)
7	Equisetin	-	*F. equiseti* and *F. semitectum*	Toxic to mice, affects Human immunodeficiency8virus and gram-positive bacteria	(Desjardins 2006)
8	Fusarins	-	*F. graminearum* and *F. verticilliodes*	Cause mutation	(Desjardins 2006)
9	Fusaproliferin	-	*F. subglutinans* and *F. proliferatum*	It causes toxicity in Artemia Salina, human B lymphocytes and in insect cells as well as it has pathogenic effects on embryos of chicken	(Marin *et al.*, 2013)
10	Moniliformin		*F. avenaceum, F. tricinctum, F. verticillioides, F. subglutinans*, and *F. proliferatum*	Cause interruption of gluconeogenesis and inhibit glutathione peroxidase and reductase	(Chen and Yang, 1990; Pirrung and Singh, 1996)

chemical agents. However, this approach is not widely employed due to the potential adverse effects on crops, rendering them unsuitable for human consumption. The detoxification of mycotoxins is accomplished using a variety of chemical processes, including acidification, ammoniation, oxidation, bases, sodium bisulfite (reducing agents), and enzymatic destruction (Munkvold *et al.,* 2019). One extensively researched approach for the management of mycotoxins via chemical methods is the utilization of ammonia or ammonium hydroxide for treating contaminated items. According to Charmley and Prelusky (1994), the use of a 2% ammonia treatment resulted in a significant decrease of up to 79% in fumonisin contamination levels in the tested items. The application of calcium or sodium hydroxide treatments has demonstrated significant efficacy in the detoxification of feeds that have been contaminated by aflatoxins, T-2, zearalenone, and diacetoxyscirpenol. The extent of detoxification, ranging from 45% to 99%, is contingent upon both the specific toxin and the moisture content of the feed (Karlovsky *et al.,* 2016). In animal-feed corn, sodium bisulfite treatments have been beneficial for mitigating deoxynivalenol, while ozone and chlorine gas treatments have been beneficial for detoxifying various mycotoxins in corn but not in wheat (Young 1986; Young *et al.,* 1986). The efficacy of formaldehyde and ammonium hydroxide in decontaminating zearalenone in maize and corn grits has been demonstrated (Charmley and Prelusky, 1994). However, it has been found that the products treated with formaldehyde are not suitable for human consumption due to their instability.

***Fusarium* as Plant Pathogens:** Presently, a total of 25,755 papers on *Fusarium* species can be found in the PubMed Central database. *Fusarium* is one of the fungal genera that is considered to be among the most economically significant in the world. At least 300 phylogenetically different species are associated with the genus (Aoki *et al.,* 2013). To this day, nine monotypic lineages and twenty species complexes have been recognized within the genus. Most *Fusarium* species are soil-dwelling fungi, but *Fusarium* conidia can spread by the water in rain splashes and through irrigation systems (Laraba *et al.,* 2022). When *Fusarium* conidia dry out, they become airborne, which makes them well-suited to travel long distances through the air and contributes to their worldwide distribution. The spread of *F. verticillioides* by insects is much less common, but it is still an extremely significant component of the entire procedure. The fungi known as *Fusarium* are classified as hemi-biotrophs, but they can transform into necro-trophs in response to certain metabolic and environmental cues. This is despite the fact that *Fusarium* employs several infection tactics (Proctor *et al.,* 2022). Among commercially important crop species, they cause root and stem rot, vascular wilt, and fruit rot, which cause yield reductions (MT ha-1) and losses of more than $1 billion (Table 2) (Attia *et al.,* 2023; Nikitin *et al.,* 2023).

The life cycle of *Fusarium spp.* : *Fusarium* spp. reproduces by both sexual and asexual means. Some *Fusarium* spp. produce ascospores (sexual and meiotic) and three kinds of asexual spores (mitotic), like chlamydospores, microconidia, and macroconidia. These spores are produced within or on hyphae, from conidiophores and sporodochium, respectively (Dweba *et al.,* 2017). In both types of reproductive stages, mycelium is haploid and spores are airborne, which may be responsible for the production of mycotoxins and infection in plants (Fig. 1). Not both types of spores (sexual and asexual) are produced by all species of *Fusarium*, and only less than 20% of species are known for their sexual life cycle (Shabeer and Jamal, 2021).

Sexual state of *Fusarium*: On the basis of their sexual stage, *Fusarium* species are included in the phylum *Ascomycota* and various genera such as *Nectria* and *Gibberella* (Table 3) (Guarro *et al.,*1999). Teleomorph is the sexual stage of a few species, which may be both homothallic and heterothallic (Kerényi *et al.,* 2004; Patel *et al.,* 2022). The chromosome size of some species was seen under a light microscope, but the accurate number of chromosomes was not determined because of their small size. For this purpose, pulsed-field gel electrophoresis (PFGE) has been used (Suga and Hyakumachi, 2004).

Pathogenicity factors of *Fusarium*: For the initiation and development of infection in host plants, different pathways are used by *Fusarium* species, such as toxins, cellular signaling pathways, and enzymes, which may include Ras proteins, velvet complexes, cAMP pathways, G-proteins, MAPKs, and cell wall-degrading enzymes, to get entry into host plants and cause infection (Koch *et al.,* 2013). These pathogenicity factors may be host-specific or may be used by different *Fusarium* species (Poppenberger *et al.,* 2003). Furthermore, it is quite concerning when new Fusarium metabolites are found in food crops and products. Food crops have been shown to contain *Fusarium* spp. which have been linked to the production of new mycotoxins such as *fusaproliferin*, *enniatins*, *beauvericin*, moniliformin, and others and are creating serious problems in numerous parts of the world (Křížová *et al.,* 2021; Oueslati *et al.,* 2011; Santini *et al.,* 2012). *Fusarium* mycotoxins are ubiquitous in crops and food products, which has led to ongoing efforts to understand their chemical structures in order to reduce the risk they pose to human and animal health. Previous research found a contradiction between animal mycotoxicosis symptoms and the comparatively low mycotoxin concentration found in the associated feed (Ekwomadu and Mwanza, 2021; Magnoli and Cavaglieri, 2019). Unidentified conjugated or mask mycotoxins, which may hydrolyze in the animals' digestive tracts and produce parent poisons, are thought to be the source of the unexpectedly high toxicity. Because there is little information on contamination and less is known about the toxicological characteristics of masked mycotoxins, it is difficult to assess the risk of these substances

Table 2. List of recent major diseases caused by Fusarium pathogen on various significant crop plants

Host plant	Pathogen	Disease	References
Watermelon	*F. oxysporum* f. sp. *niveum* (*Fon*)	*Fusarium* wilt	(Noman *et al.*, 2023)
Ginger	*F. oxysporum* f. sp. *zingiberi* (*Foz*)	*Fusarium* yellows of ginger	(Prasath *et al.*, 2023)
Wheat	*F. pseudograminearum*	*Fusarium* crown rot	(Wei *et al.*, 2023)
Wheat	*F. graminearum*	*Fusarium* head blight	(Zhang *et al.*, 2023)
Chickpea	*F. oxysporum* f. sp. cicero	Wilt of chickpea	(Harsha *et al.*, 2023)
Banana	*F. oxysporum* f. sp. *cubense* (Foc)	*Fusarium* wilt	(Lishma *et al.*, 2023)
Tobacco	*F. redolens*	Tobacco *Fusarium* Root Rot	(Gai *et al.*, 2023)
Sugarcane	*Fusarium* spp.	Twisted top disease	(Viswanathan *et al.*, 2023)
Maize	*F. moniliforme*	Ear rot disease	(Mishra and Arora, 2022)
Sweet pepper	*F. oxysporum* f. sp. *capsici*	*Fusarium* wilt	(El-Nagar *et al.*, 2022)
Cotton	*F. oxysporum* f. sp. *vasinfectum*	*Fusarium* wilt	(Zhu *et al.*, 2022)
Lettuce	*F. equiseti*	Foliar disease of Lettuce	(Tziros and Karaoglanidis, 2022)
Cowpea	*F. oxysporum* f. sp. *Tracheiphilum*	*Fusarium* wilt	(Dong *et al.*, 2022)
Potato	*F. sulphureum*	Dry rot of potato	(Li *et al.*, 2022)
Apple	*F. proliferatum* f. sp. *malus domestica*	Apple Replant Disease	(Duan *et al.*, 2022)
Cucumber	*F. oxysporum* f. sp. *cucumerinum*	Wilt	(Sun *et al.*, 2022)
Tomato	*F. oxysporum* f. sp. *lycopersici*	Wilt	(Jin *et al.*, 2022)
Watermelon	*F. oxysporum* f. sp. *niveum*	Wilt	(Lv *et al.*, 2022)
Pumpkin	*F. oxysporum* f. sp. *cucumerinum*	Wilt	(Xu *et al.*, 2022)
Lettuce	*F. oxysporum*	Wilt	
Tomato	*F. solani*	Damping off	(Hamed and Alhewairini, 2022)
Saposhnikovia divaricata	*F. equiseti*	Root rot	(Han *et al.* 2022)
Bael	*F. pallidoroseum*	Leaf spot	(Jayalakshmi *et al.*, 2022)
Chrysanthemum morifolium	*F. oxysporum*		(Guan *et al.*, 2022)
Watermelon	*F. equiseti*	*Fusarium* Wilt	(Han *et al.*, 2022)
Kiwifruit	*F. breve*	Root rot	(Cui *et al.*, 2023)
Dendrobium officinale	*Fusarium* spp.	Diebacz	(Mirghasempour *et al.*, 2022)
Apple	*F. solani*	Apple replant disease	(Xiang *et al.*, 2021)
Papaya	*F. incarnatum*	Fruit rot of papaya	(Bachkar *et al.*, 2021)
Mango	*F. neocosmosporiellum*	Mango malformation	(Molina-Cardenas *et al.*, 2021)
Hot pepper	*F. oxysporum* f. sp. *capsici*	*Fusarium* wilt	(Shaheen *et al.*, 2021)
Potato	*Fusarium* spp.	Tuber dry rot	(Khedher and Tounsi, 2021)
Cereal crops (maize)	*F. verticillioides*	Stalk rot	(Yu *et al.*, 2021)
Sesame	*F. oxysporum* sp. *sesami*	Damping off	(Hassan *et al.*, 2021)
Cashew	*F. oxysporum*	Wilt	(Mbasa *et al.*, 2021)
Onion	*F. proliferatum*	*Fusarium* basal rot	(Leand Haesaert, 2021)
Citrus	*F. solani*	Dry root rot	(Ezrari *et al.*, 2021)
Passion Fruit	*F. nirenbergiae*	Wilt	(Aiello *et al.*, 2021)
Melon	*F. incarnatum-equiseti*	*Fusarium* rot	(Lima *et al.*, 2021)
Loquat	*F. solani*	Root Rot	(Wu *et al.*, 2021)
Mango	*F. oxysporum*	Mango maturity malconformation	(Kausar *et al.*, 2021)
Cannabis	*F. lichenicola*	Crown rot	(Punjaand Roberts, 2021)
Blackberry	*F. cugenangense*	Wilt	(Kim *et al.*, 2021)
Chinese cherry	*Fusarium* spp.	*Fusarium* rot	(Wang *et al.*, 2021)
Date palm	*F. proliferatum*	Leaf wilt	(Ghaedi *et al.*, 2020)
Strawberry	*F. oxysporum* f. sp. *fragariae*	*Fusarium* wilt of strawberry	(Henry *et al.*, 2020)
Guava	*F. oxysporun* f.sp. *psidii*	Sudden decline	(Singh 2020)
Strawberry	*F. oxysporum*	*Fusarium* wilt	(Li *et al.*, 2019)
Chickpea	*F. oxysporum* f. sp. *ciceri*	*Fusarium* wilt	(Anusha *et al.*, 2019)
Mung bean	*F. oxysporum*	Mung bean wilt	(Sun *et al.*, 2019)
Cotton	*F. oxysporum* f. sp. *vasinfectum*	Wilt	(Wei *et al.*, 2019)
Peanut	*F. solani*	Root-rot	(Li *et al.*, 2018)
Rice	*F. fujikuroi*	Rice bakanae disease	(Hou *et al.*, 2018)
Tomato	*F. oxysporum* f. sp. *lycopersici*	Wilt	(Elanchezhiyan *et al.*, 2018)
Sweet potato	*F. solani*	*Fusarium* root rot	(Yang *et al.*, 2018)
Cucumber	*F. oxysporum* f. sp. *cucumerinum*	*Fusarium* wilt	(Raza *et al.*, 2017)
Onion	*F. oxysporum* f. sp. *cepae*	Basal rot	(Javaid *et al.*, 2017)
Garlic	*F. proliferatum*	Bulb rot	(Patón and Llamas, 2017)
Pea	*F. avenaceum*	Root rot	(Šišićand Finckh, 2017)
Cabbage	*F. oxysporum* f. sp. *conglutinans*	Cabbage yellows	(Kashiwa *et al.*, 2016)

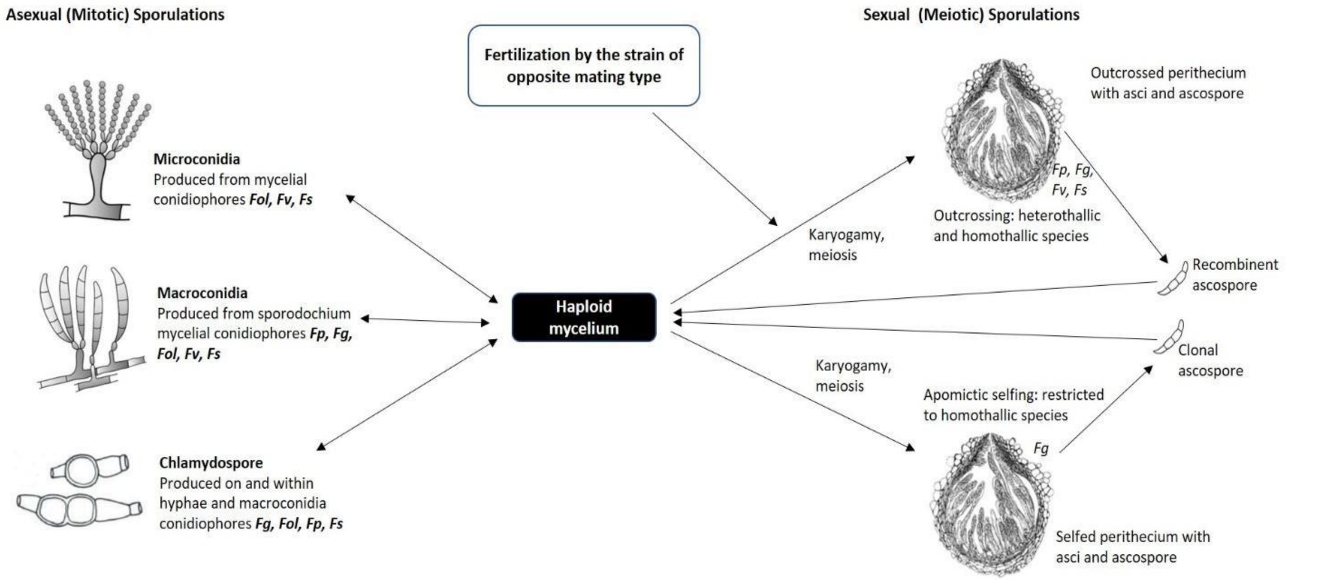

Figure 1. The General life cycle of *Fusarium* spp. karyogamy and plasmogamy results in the development of recombinant and clonal sexual spores in the selfed perithecium and outcrossed which in turn forms haploid mycelium.

in food. It has become important to comprehend the toxic effects of hidden mycotoxins and assess the risks brought on by the co-presence of target mycotoxins in food products (El-Sayed *et al.*, 2022). To ensure the protection of consumer health and carry out thorough assessments of the health hazards posed by these mycotoxins, food producers, risk assessment and monitoring authorities, and other studies address this issue (Yong *et al.*, 2023; Keskin and Eyupoglu, 2023).

FUSARIUM MYCOTOXIN PRODUCTION AND TOXICITIES

There are three main classes of mycotoxins produced by *Fusarium* spp. such as zearalenones with their mycoestrogens, fumonisins, and trichothecenes (Fig. 2) (Xue and Yang, 2023). These metabolites are carcinogenic in nature, exert devastating effects on animal health, and are responsible for birth defects and esophageal cancer in humans (El-Sayed *et al.*, 2022; Wang *et al.*, 2023).

Trichothecenes: Trichothecens are toxic substances consisting of more than 200 different types. They are not produced by the *Fusarium* species but are structurally similar to the fungal secondary metabolites (Janik *et al.*, 2021). They are a family of naturally occurring tetracyclic sesquiterpenoids and part of a class of terpenes consisting of three isoprene units. Structurally, they consist of an epoxide group, an olfenic group, and variable numbers of acetyl and hydroxyl groups (Polak-Śliwińska and Paszczyk, 2021). Based on functional groups, trichothecenes are categorized into four groups, namely A, B, C, and D (Agriopoulou and Varzakas, 2020; Gruber-Dorninger and Schatzmayr, 2019). Among them, A and B are the most significant and highly toxic food substances. In type A trichthecenes, highly toxic T2 toxin is present in its different deacetylated forms, such as neosolaniol (NEO), diacetoxyscirpenol (DAS), and HT-2 toxin (HT-2) (Zhang *et al.*, 2018). However, type B trichothecenes include nivalenol (NIV), deoxynivalenol (DON), and their acetylated derivatives such as fusarenon-X (FUS-X), 15-acetyldeoxynivalenol (15-ADON), and 3-acetyldeoxynivalenol (3-ADON) (Müller *et al.*, 1997). Trichothecenes contaminate the cereal crops in all growing regions of the world (especially FUS-X), which are consumed by humans and livestock or animals, including wheat, oats, barley, and maize (Foroud and Eudes, 2009; Placinta and Macdonald, 1999). They inhibit protein synthesis in eukaryotes by interfering with their initiation, elongation, and termination stages. These toxins are involved in different diseases in humans and animals, such as blood disorders, vomiting, feed refusal, weight loss, disturbance of the nervous system, abortions, nausea, hemorrhaging of internal organs, immunosuppression, and inflammation of the skin. Type A atrichothecenes are associated with neurotoxicity, cytotoxicity, and immunotoxicity, while type B trichothecenes are related to the most important functional manifestations like gastrointestinal disorders, reduced weight gain, and emesis (Ekwomadu and Mwanza, 2021). Trichothecens have been noticed to be toxic to all humans and animals, but their sensitivity varies depending on the species and toxins, and the most sensitive farm animal to toxins is swine. In humans, clinical gastrointestinal treatments are most commonly observed because the first target tissue for toxins

Table 3. Teleomorph (asexual) state of Fusarium species with their known sexual state.

Sr.	Asexual/Anamorph	Sexual/Teleomorph	References
1	*F. roseum* var. *avenaceum*	*Gibberellaavenacea*	(Cook 1967)
2	*F. moniliforme*	*G. fujikuroi*	(Chang and Sun, 1975)
3	*F. Lateritium*	*G. Baccata*	(Afanide and Naqvi, 1976)
4	*F. udum*	*G. indica*	(Rai and Upadhyay, 1982)
5	*F. solani*	*Nectriahaematococca*	(Windels 1991)
6	*F. sambucinum*	*G. pulicaris*	(O'Donnell 1992)
7	*F. acuminatum*	*G. acuminata*	(Elmer 1996)
8	*F. pseudograminearum*	*G. coronicola*	(Aoki and O'Donnell, 1999)
9	*F. heterosporum*	*G. gordonii*	(Sheraliev and Bukharov, 2001)
10	*F. verticillioides*	*G. moniliformis*	(Jurgenson and Leslie, 2002)
11	*F. sacchari*	*G. sacchari*	(Leslie *et al.*, 2005)
12	*F. xylarioides*	*G. xylarioides*	(Geiser *et al.*, 2005)
13	*F. circinatum*	*G. circinata*	(Gordon *et al.*, 2006)
14	*F. proliferatum*	*G. intermedia*	(Salvalaggio and Ridao, 2013)
15	*F. gibbosum*	*G. intricans*	(Dutkiewicz *et al.*, 2016)
16	*F. graminearum*	*G. zeae*	(Khan *et al.*, 2020)

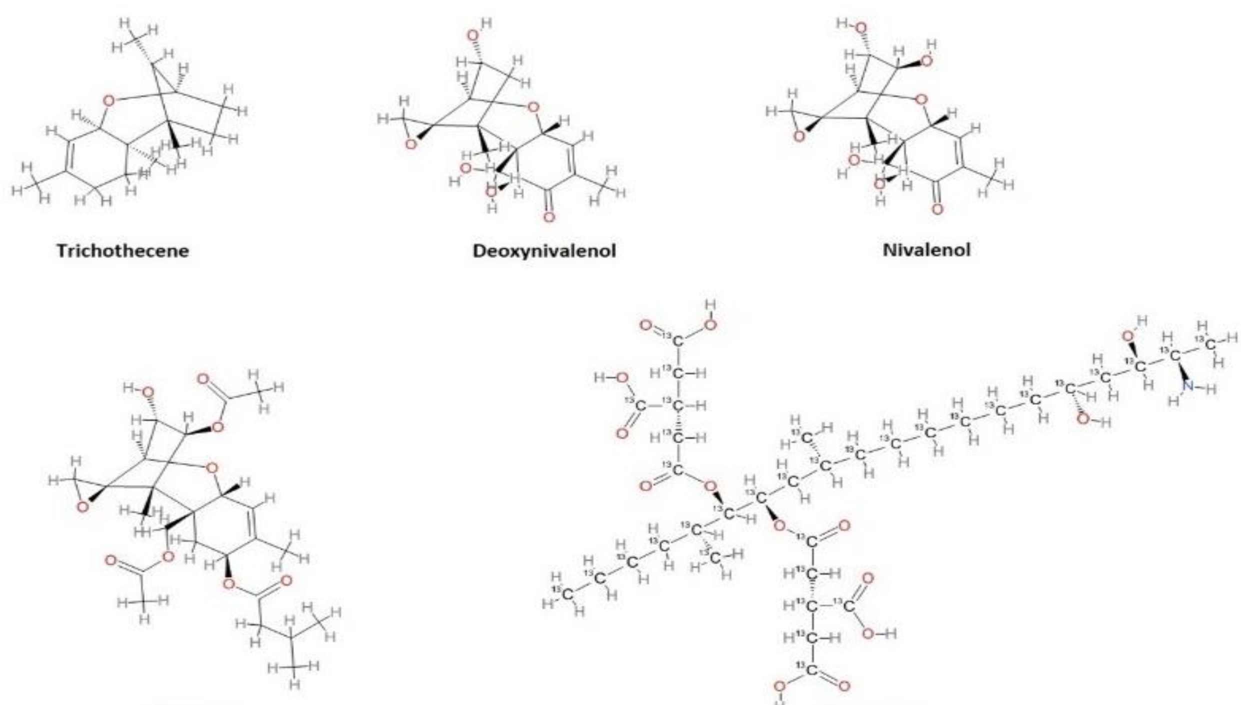

Figure 2. Structural depiction of some well-known mycotoxin produced from the Fusarium species.

is the intestinal epitheium (Islam and PESTKA, 2008; Pierron *et al.*, 2022).

***Deoxynivalenol*:** Deoxynivalenol (DON) is produced in different geographical areas and regions by *Fusarium* culmorum or *Fusarium* graminearum. It is also termed vomitoxin and may be associated with zearalenone because both of them are produced by the same *Fusarium* species (Richard 2000). The most commonly affected grains by DON include wheat, maize, barley, and oats. These toxic substances have been classified as the 3rd group and cannot be reclassified concerning their carcinogenic effects on human health. In animals, DON is associated with different disorders and diseases, such as decreased milk in dairy cattle and swine feed refusal because of unpalatable feed or vomiting due to the consumption of contaminated feed. In various species of animals, reduced feed intake causes severe weight loss, which may lead to immune system disorders and disturb their reproductive capacity. Similar symptoms of vomiting are also reported in human beings due to the consumption of DON-contaminated grains (Ekwomadu and Mwanza, 2021).

Furthermore, due to the consumption or use of DON-contaminated wheat bread over a week, severe infections of the upper respiratory tract have been reported in children, and illness decreased with stopped bread ingestion. DON's toxicity is supposed to occur due to the modulation or disruption of the innate immune system. Short-term exposure to a high dosage of DON may result in emesis, shock-like conditions, and gastroenteritis, while long-term exposure to a low dosage may cause fluctuations in the production of IgA and growth hormones, reduced weight loss, and anorexia (Hopton *et al.,* 2010; Pestka, 2010). There are no residual amounts of DON's in the fluids and tissues of animals that are exposed to their toxic levels, but maltin and the baking of contaminated barley and wheat may exert devastating effects (Richard 2000).

***Nivalenol*:** Nivalenols are trichothecens, which are produced by the *Fusarium* species and are responsible for pig diseases. Contaminated food results in feed refusal because the food is unpalatable and may lead to vomiting (Agag 2005). Nivalenol exerts no harmful effects on chickens; cattle show resistance against some diseases caused by it; and in the case of pigs, the maize rations should not contain more than 5% of contaminated kernels. These toxic substances have been classified as the 3rd group and cannot be reclassified concerning their carcinogenic effects on human health (Kumar *et al.,* 2022).

***T-2 toxins*:** T-2 toxins cause changes in the reproductive organs and weaken the functions of the immune system by causing a delay in the regeneration of spleen and bone marrow cells (Paterson and Lima, 2010). Different types of disorders and symptoms, such as loss of appetite, weight loss, abortion, poor or reduced feed consumption, bloodstained diarrhea, and vomiting, are expressed by the infected animals, and in severe cases, these problems may lead to death. They are also responsible for necrosis, hemorrhage, and irritation throughout the gastrointestinal tract (GIT) (Agag 2005). In Russia, thousands of people were killed by alimentary toxic aleukia (ATA), which was caused by T-2 toxins. It also suppresses the immune system, causes necrosis, and has other cytotoxic impacts. ATA induces different symptoms, including nose bleeding, fever, and bleeding from the gums, skin, and throat (Zain 2011).

***Fumonisins*:** Fumonisins are carcinogenic and cytotoxic mycotoxins, and they were discovered for the first time in 1988 (Gelderblom *et al.,* 1988). Fumonisin analogues are divided into four series named A, B, C, and P. Till now, 28 structurally related fumonisin analogues have been discussed. Among all of them, the most significant mycotoxin in contaminated maize is fumonisin B, which also occurs naturally. Toxicologically, analogs of fumonisin B consist of the three most important fumonisins, such as B1, B2, and B3, which are also referred to as Bs fumonisins (Marasas 1996). Bs fumonisins abundantly occur in nature, with the highest concentration of B1. B1 is produced by *F. verticillioides*, a fungal pathogen of maize that was previously known as *F. moniliforme*. In humans, B1 is associated with esophageal cancer in different countries, including Northeast Italy, China, and the Transkei region of South Africa, which is caused by the consumption of maize contaminated with fumonisin (Peraica *et al.,* 2000).

Marasas (1996) have documented that in babies, FB1 has been linked to neural tube abnormalities as a result of its capacity to reduce folate absorption in different cell lines. In the vicinity of the Texas-Mexico border, it has been documented that fumonisin B1 can lead to the occurrence of neural tube abnormalities in infants born to moms who have consumed maize contaminated with this substance (Sadler *et al.,* 2002). Impaired growth in children has been found to be connected with chronic consumption of fumonisin mycotoxins. As per the International Agency for Research on Cancer (IARC), FB1 has been classified under Group 2B, indicating its potential toxicity to humans. Fumonisin B1, which shares structural similarities with sphingoid bases, can elucidate the mechanism by which the manufacture of sphingolipid complexes is hindered, resulting in cellular damage and ultimately cell demise. Fumonisins have a certain degree of resistance to heat, although it should be noted that in heat-treated food products, FB1 is present in chemically bonded states (Braun and Wink, 2018). In contrast to other widely recognized mycotoxins that exhibit solubility in organic solvents, fumonisins possess water solubility, hence presenting a significant obstacle in terms of their investigation.

EMERGING MYCOTOXINS

Despite the limited body of research about this topic, there has been a notable surge in scholarly attention to developing mycotoxins in recent times. Mycotoxins have the potential to coexist with many other toxins, such as free and modified mycotoxins, in regions where crops are grown that are susceptible to *fusarium* contamination (Jestoi 2008). *Fusarium* infection can be ubiquitously found in agricultural areas where crops are cultivated. Based on the available literature, it has been observed that certain developing mycotoxins are present in substantial quantities. In the subsequent sections, we will thoroughly examine each toxin (Fig. 3).

***Beauvericin* (BEA):** Various species of *Fusarium* are known to produce a cyclic depsipeptide known as BEA (Jestoi, 2008). The frequent simultaneous presence of this substance in food and feed alongside other mycotoxins gives rise to significant concerns. Although there is currently no established link between this metabolite and mycotoxicoses, it is crucial to acknowledge that the existing body of research on the toxicity of BEA is primarily limited to in vitro experiments. The toxicity of BEA arises from its possession of ionospheric characteristics and its ability to inhibit enzymes, resulting in apoptosis in several cell lines (Jajić *et al.,* 2019). BEA has been found to exhibit phytotoxic

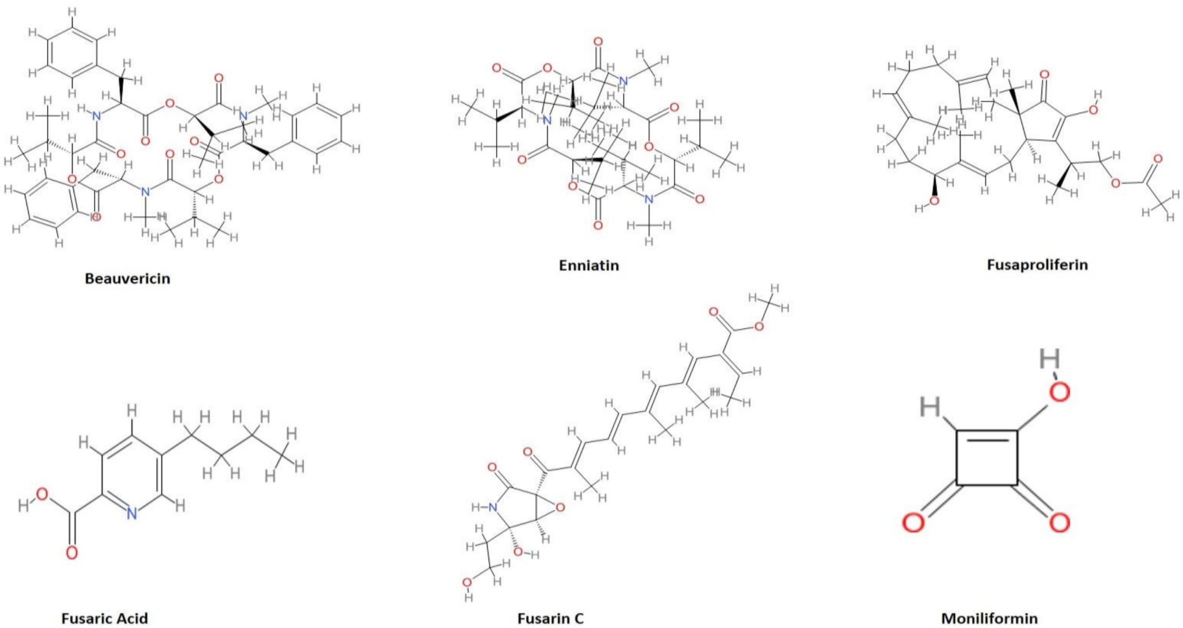

Figure 3. Emergıng mycotoxıns and their structural form

properties and contribute to the pathogenicity of *F. oxysporum* on tomato plants (López-Díaz *et al.,* 2018; Perincherry and Stępień, 2019).

Enniatin **(ENN):** Cyclodepsipeptides, known as ENN mycotoxins, are created by individuals from different species complexes (Urbaniak and Stępień, 2020). ENNs and BEA share a similar structural makeup and are produced by the same nonribosomal peptide synthase (Munkvold and Moretti, 2021). ENNs have been shown in laboratory tests to be capable of disrupting the cell cycle, causing lipid peroxidation, and causing mitochondrial malfunction (Prosperini *et al.,* 2017). ENNs can also damage cell membranes by creating pore structures that make them more permeable. ENNs are regularly found in human urine, according to one investigation, underscoring the high frequency of exposure to people. The pathogenicity of *F. avenaceum* on potato tubers is aided by ENNs, host-nonspecific phytotoxins that can affect a variety of plants (Eranthodi *et al.,* 2020).

Fusaproliferin **(FUP):** FUP, a bicyclic sesterterpene, was first identified in *Fusarium* proliferatum, and all organisms capable of producing FUP are associated with the F. fujikuroi species complex (Munkvold and Moretti, 2021). The primary harmful effect of FUP has been proven to be teratogenicity in chicken embryos (Moretti *et al.,* 1997). Instances of *Fusarium* mycotoxin contamination in maize have been documented in several regions, including South Africa, the United States, and European countries. Moreover, *Fusarium* mycotoxins are commonly accompanied by FUP (Bottalico 1998).

Fusaric Acid**:** Fusaric acid exhibits a moderate level of acute toxicity towards mammals and is produced by several complexes of *Fusarium* species. Recent research has revealed that fusaric acid can enhance the toxicity of many other mycotoxins produced by the *Fusarium* species, such as deoxynivalenol (DON), fumonisins (FUMs), T-2 toxin, and zearalenone (ZEA) (Bacon *et al.,* 1996; Berthiller *et al.,* 2013). The potential adverse impacts of fusaric acid, when combined with highly toxic mycotoxins, are likely to be more pronounced compared to the consequences solely attributed to fusaric acid. Moreover, it has been shown that fusaric acid exhibits phytotoxic properties and is associated with the ability of certain formae speciales (f. sp.) of *F. oxysporum* to induce wilt symptoms in particular crops (Gopalakrishnan and Srinivas, 2016; Srinivas *et al.,* 2019). Nevertheless, previous investigations on gene deletion have shown that the inhibition of fusaric acid synthesis did not significantly mitigate the pathogenic effects of *F. oxysporum* on cactus or *F. verticillioides* on maize (Munkvold and Moretti, 2021).

Fusarin **C:** Fungal-derived secondary metabolites, known as fungal polyketides, consist of a polyketide core structure that undergoes various modifications on a 2-pyrrolidone functional group. FUS C, the initial FUS counterpart to be identified, was obtained by the purification process from a strain of F. verticillioides that induced bacterial mutations (Proctor *et al.,* 2006). Fumonisins (FUSs) have not been associated with established mycotoxicoses in people or animals. However, it has been observed that FUS C can induce chromosomal damage in mammalian cell cultures (Ismaiel and Papenbrock, 2015). In specific groups of species, there is variation in the creation of FUS, with some species exhibiting this production while others do not. Additionally, certain species that produce FUS also synthesize TRIs and

FUMs (Brown *et al.,* 2012). The precise understanding of the natural presence of FUSs in grain, feed, or diet remains limited.

***Moniliformin*:** The presence of a commonly occurring metabolite known as MON has been associated with several instances of mycotoxicoses in animals, with a particular emphasis on poultry (Jestoi 2008). Previous studies have provided evidence of the toxin's ability to impede protein synthesis, induce cytotoxicity, and inflict damage on chromosomes. The experimental animals and poultry have shown a correlation between exposure to MON and several adverse effects, including lower body weight, intestinal hemorrhaging, unconsciousness, and mortality (Munkvold *et al.,* 2021). *Fusarium* species, specifically those belonging to the *F. fujikuroi* species complex such as *F. fujikuroi*, *F. proliferatum*, and *F. nygamai*, are known to produce a significant amount of MON (Bashyal *et al.,* 2019; Pena and Chulze, 2019). However, it should be noted that F. verticillioides does not exhibit this characteristic. It is noteworthy to mention that certain animals that produce TRI also generate MON.

MASKED MYCOTOXINS

Masked mycotoxins are mycotoxins that undergo modifications by plant enzymes and are often conjugated with more polar metabolites, such as sugars (Berthiller *et al.,* 2013). The structural modifications of mycotoxins are employed by plants as a defense mechanism against xenobiotics. Plants can modify mycotoxins through many mechanisms, with glycosylation being the predominant one, involving the conjugation of glucose (Freire and Sant'Ana, 2018). Masked mycotoxins are carried to vacuoles within plants, where they undergo storage or conjugation processes with biopolymers, such as the constituent components of cell walls (Munkvold and Moretti, 2021). Standard mycotoxin screening approaches commonly failed to detect conjugated mycotoxins, resulting in the concealment of this phenomenon. Masked mycotoxins have the potential to accumulate in the consumable portions of crops infected with *Fusarium*, often coexisting with unmodified mycotoxins at elevated levels. Despite being generally less detrimental than unmodified mycotoxins, masked mycotoxins can nevertheless pose a risk. The absence of sufficient understanding of the toxicological properties of masked mycotoxins has resulted in the absence of established maximum allowable levels. During the process of mammalian digestion, certain mycotoxins that were previously concealed may transform, becoming free and readily available. Extensive research has been conducted on the concealed forms of *Fusarium* mycotoxins, particularly focusing on FUMs in maize (Janić Hajnal *et al.,* 2023; Ostry *et al.,* 2010), as well as DON, NIV, T-2, HT-2, and ZEA in other crops (Brodal *et al.,* 2016; Schollenberger *et al.,* 2006). Berthiller *et al.* (2013) first noticed the metabolic biotransformation of DON to less dangerous derivatives in plants. They recovered DON-3-d-glucoside (DON-3-Glc) from maize cell suspension cultures that had been DON-treated specifically. Through conjugation with sugars, amino acids, and compounds bearing sulfate groups, new DON derivatives were subsequently produced. DON-3-Glc can be found in barley, maize, and wheat in natural amounts up to 70% of the DON concentration (Kostelanska *et al.,* 2009). Furthermore, DON-3-Glc has been found in alcoholic beverages, breakfast cereals, and snacks (Crews and MacDonald, 2015; Vaclavikova *et al.,* 2013). The main changes in T-2 in plants include glycosylation of the 3-hydroxyl group as well as conjugation with malonic and ferulic acids. Worldwide, grains have been shown to contain HT-2 and T-2 compounds, including HT-2-3-glucoside and T-2-3-sulfate (Juan and Mañes, 2013; Pierzgalski *et al.,* 2021). In wheat and maize cell cultures as well as in barley treated with ZEA, the production of glycosylated forms of ZEA has been noted (Munkvold and Moretti, 2021).

PROGRESS IN DETOXIFICATION

Being heat-stable chemicals, mycotoxin reduction in numerous agricultural commodities is currently a big challenge in many countries (Agriopoulou and Varzakas, 2020; Awuchi *et al.,* 2022). Several preventive measures have been put in place to allay these worries, including pre-harvesting practices intended to stop the growth of toxic fungus and the creation of mycotoxins, as well as post-harvesting tactics intended to detoxify food once mycotoxins have been produced (Afsah-Hejri and Ehsani, 2020; Awuchi *et al.,* 2021). However, none of these steps can eliminate mycotoxins from diet or feed. However it is crucial to reduce mycotoxin prevalence below the level at which it has a negative economic impact, which is why so many studies try to address these issues. Numerous methods, such as prevention and decontamination mechanisms, have been investigated for reducing mycotoxin formation and limiting fungal growth in a variety of crops. Good agricultural practices (GAPs), good manufacturing practices (GMPs), and good hygienic practices (GHPs) are among the strategies used to avoid fungus development and the production of mycotoxin, whereas the majority of decontamination methods use chemical, physical, and biological methods (Bryła *et al.,* 2022; Sujayasree *et al.,* 2022). Crop rotation, tillage, pesticide application, and adaptation of the sowing window or usage of resistant hosts are a few examples of agricultural practices; physical techniques (cleaning, sorting, irradiation, thermal or ultrasound treatment, temperature and humidity control); chemical approaches (acids and bases such as ammonia, hydrogen peroxide, or antifungal agents); and biological control methods made of the use of microorganisms (bacterial, yeast, and fungi) and plant products (plant essential oils, plant extracts, etc.) (Hamad *et al.,* 2022; Wielogorska *et al.,* 2019). Although chemical and physical detoxification methods have shown potential in reducing mycotoxin formation and fungal infection, it is important to acknowledge the various limitations, challenges, and problems associated

with these approaches. Chemical methods may at times necessitate the use of specialist equipment and costly chemicals or the implementation of harsh treatment conditions. These factors can potentially result in adverse effects on the environment and non-targeted organisms, which are undesired. Physical techniques frequently exhibit a deficiency in both specificity and efficacy. Moreover, it is commonly believed that a number of the methodologies are deemed impracticable, costly, ineffective, laborious, or time-intensive (Alabouvette *et al.*, 2009; Wielogorska *et al.*, 2019). Furthermore, they have the potential to pose health risks to both humans and animals. Moreover, the potential hazard posed by fungicide-based approaches is compounded by the fact that numerous antifungal chemical compounds exhibit poor biodegradability or sluggish degradation rates. Consequently, these compounds can contaminate both soil and water, adversely impacting food quality and posing risks to both human health and the environment. According to da Cruz *et al.* (2013), the extended application of chemical treatments on grains can result in the emergence of fungal strains that are resistant to these treatments. As a consequence, higher doses of chemicals may be necessary, hence augmenting the presence of detrimental residues in food crops. Nevertheless, with the increasing awareness among consumers regarding the potential hazards associated with chemicals in the food chain, there is a growing implementation of legislation aimed at regulating the use of chemical control methods. Consequently, there is a societal and ecological transition towards the consumption of natural and chemical-free food, which is neither treated nor preserved using chemical substances. Biological approaches have garnered heightened interest due to their various advantages, including target selectivity, economic feasibility, and environmental safety (Guan *et al.*, 2021; Hathout and Aly, 2014; Ji and Zhao, 2016; Yao and Long, 2020). This section presents a thorough evaluation of the latest biological methods employed for the detoxification of these mycotoxins.

BIOLOGICAL DETOXIFICATON

To combat *Fusarium* spp. and their corresponding mycotoxins, many pre-harvest and post-harvest biological management techniques have been developed for significant crops. These have utilized a range of biological control agents (BCAs), such as bacterial and fungal strains, toxigenic fungal strains, and botanicals (essential oils, raw plant extracts, or phenolic acids) (Azeem *et al.*, 2020). Although this discipline is still in its infancy, the majority of reported BCAs are still restricted to the in vitro lab scale and are not routinely commercialized. To ensure optimal integration, several factors still need to be researched. Understanding the mechanisms that control the interaction of BCAs and pathogens throughout time is particularly crucial. There are four typical ways that BCAs work that has been recognized and reported by numerous researchers: Competition for nutrients or niches, mycoparasitism, and stimulation or increase of plant defense are all examples of antibiosis (Błaszczyk *et al.*, 2017; Błaszczyk *et al.*, 2023; Pellan *et al.*, 2021). The presence of one dominant mode of action does not preclude the presence of others; modes may vary depending on the characteristics and kinds of BCAs being considered. BCAs often rely on multiple modes of action to combat the pathogen. Even though numerous BCAs have been synthesized and their effective usage in the battle against mycotoxigenic fungi has been documented, the following paragraphs will only examine a few due to the significance of these BCAs for long-term defense against *Fusarium* spp.

***Trichoderma* as Biological Detoxifying Organisms:** Trichoderma refers to a group of filamentous fungi that are capable of independent existence and are commonly found in soil. Certain strains of Trichoderma can colonize the rhizosphere, which is the region of soil surrounding plant roots, thereby establishing a symbiotic relationship with root ecosystems (Ali et al., 2021; Yumeng *et al.*, 2023; Li *et al.*, 2023). Extensive research has been conducted on the capacity of the Trichoderma genus to effectively counteract plant pathogenic fungus. The biological control mechanisms of this organism primarily encompass enhanced growth rates and the production of antibiotics to outcompete pathogens for resources and habitat, mycoparasitism facilitated by the secretion of enzymes that degrade cell walls, and the ability to stimulate plant defense systems (Anwaar et al., 2022; Pellan *et al.*, 2021). The effects of Trichoderma spp. Biocontrol can be categorized into direct and indirect impacts. Direct effects encompass several mechanisms, such as nutrition and space competition, the synthesis of lytic enzymes and volatile/nonvolatile antibiotics, the deactivation of pathogen enzymes, and parasitic interactions. Indirect effects in host plants encompass various phenomena, such as adaptation to stress, solubilization or sequestration of inorganic nutrients, and development of resistance against fungal phytopathogens (Ren *et al.*, 2022). Trichoderma species are efficient bio-controllers of phytopathogenic *Fusarium* (Zin and Badaluddin, 2020). These species possess the potential to integrate multiple benefits into a single product, including the prevention of diverse plant diseases, the promotion of plant growth, and the enhancement of the agricultural environment to support sustainable practices. In a screening experiment conducted by Baszczyk *et al.* (2017), a total of twenty-four isolates belonging to ten different Trichoderma species were investigated for their ability to suppress the growth of mycelium and production of mycotoxins by five strains of *Fusarium*. On the fourth-day post-co-inoculation, upon the initial observable physical interaction between the antagonist and pathogen, it was seen that all selected strains had the ability to impact the mycelial growth of a minimum of four out of the five *Fusarium* species under investigation. Baszczyk *et al.* (2017) revealed that the synthesis of toxins by all five *Fusarium* species, namely *F. avenaceum*, *F. cerealis*, *F. culmorum*, *F. graminearum*, and

F. temperatum, on solid substrates was significantly inhibited by *T. atroviride* AN240, resulting in a substantial reduction in toxin levels ranging from 69% to 100%. In recent times, there has been a noticeable surge in the level of attention given to the utilization of Trichoderma strains as a means of biological control to regulate the production of deoxynivalenol (DON). In a study conducted by Tian *et al.* (2016), it was observed that the application of eight Trichoderma strains resulted in a considerable inhibition of mycelial growth in *F. graminearum*. Furthermore, the presence of these strains led to a decrease in the formation of the mycotoxin DON. Furthermore, the investigation revealed that the interactions between Trichoderma and F. graminearum resulted in the identification of a modified mycotoxin known as deoxynivalenol-3-glucoside (DON-3G). Previously, DON-3G was believed to be a detoxification byproduct of deoxynivalenol (DON) in the defense mechanisms of plants. Furthermore, the research conducted by He *et al.* (2019) revealed that the biocontrol agent Trichoderma asperellum, namely the GDFS1009 isolate, exhibited a significant inhibition rate of 60% against stalk rot in maize caused by *Fusarium* graminearum. Additionally, it was discovered that the chemical exerted an influence on the growth of the maize plant. A separate investigation was conducted to analyze the effects of T. harzianum Th22 cellulase on the stimulation of 2,4-Dihydroxy-7-methoxy-2H-1,4-benzoxazin-3(4H)-one (DIMBOA) production and the expression of defense-related genes in maize roots as a defense mechanism against DON-producing F. graminearum. According to Saravanakumar *et al.* (2018), the presence of DIMBOA was observed to have a suppressive effect on the mycotoxin-related and pathogenicity proteins in the F. graminearum pathogen. A total of seven strains of Trichoderma asperellum, obtained from agricultural fields located in the southern region of China, were subjected to evaluation in terms of their efficacy against *F. graminearum*. According to Li *et al.* (2016), the *T. asperellum* ZJSX5003 strain exhibited a considerable enhancement in its antagonist activity against *F. graminearum* and resulted in a notable reduction of disease prevalence in maize plants that were inoculated, with a decrease of 71% as compared to the negative control.

Trichoderma strains have been found to exhibit the ability to attenuate various other mycotoxins. Tian *et al.* (2018) reported that three Trichoderma isolates exhibit significant efficacy in inhibiting the growth of mycelia and suppressing the synthesis of mycotoxins by ZEN-producing *F. graminearum*. In addition, the experiments conducted with ZEN-treated samples revealed that the Trichoderma isolates under investigation were unable to detoxify ZEN through glycosylation. However, they were capable of converting ZEN into its reduced forms (-ZOL and _-ZOL) as well as its sulfated metabolites (ZEN14S and ZOL14S). These findings provide further insights into the interactions between Trichoderma isolates and fungi that produce ZEN. Moreover, there has been a notable focus on strains of *T. harzianum*. In both controlled and uncontrolled environments, the introduction of *T. harzianum* T22 and Th-8 strains during maize seeding resulted in a reduction of *F. verticillioides* colonization in kernels and contamination by FBs. Additionally, this seeding approach induced systemic resistance in maize against these pathogens (Błaszczyk *et al.*, 2017). Furthermore, studies have demonstrated the efficacy of T. harzianum T16 and T23 strains as antagonists against *F. verticillioides* and FBs production in maize kernels, both in liquid and agar medium.

***Lactic Acid Bacteria as a Biological Detoxifying Agent*:** A variety of bacteria known as lactic acid bacteria (LAB) can produce lactic acid by fermenting carbohydrates. Several species, including *Streptococcus* spp. *Lactobacillus* spp. *Lactococcus* spp. and *Leuconostoc* spp. are included in this group (Agriopoulou *et al.*, 2020; Ali *et al.*, 2023). LAB are probiotics that are found naturally in food and have been proven to be either unharmful or advantageous to human health. LAB is heavily studied for mycotoxin degradation due to its high safety profile in food applications. They also create a variety of bioactive substances, such as acetic and lactic acids, hydrogen peroxide, proteinaceous substances, reuterin, hydroxyl fatty acids, and phenolic substances, which can successfully inhibit fungal development and stop the production of mycotoxins in food (Smaoui *et al.*, 2022). Lactic acid bacteria (LAB) can detoxify mycotoxins by adhering to their cell structure or by breaking them down through metabolic pathways (Li *et al.*, 2021). Fungi like *F. graminearum* or F. verticillioides can be controlled biologically by LAB in maize and during food processing. This is because LAB can stop fungi from growing and remove many mycotoxins. They are also safe and good for probiotics. It has been discovered that *Lactobacillus* spp. particularly *L. plantarum*, is particularly effective at lowering mycotoxin concentrations (Smaoui *et al.*, 2022). In one study, only L. buchneri and L. plantarum were able to lower the amount of ZEN in corn silage that had been contaminated with mycotoxigenic fungus. LAB inoculants also decreased the concentrations of DON and FB1 mycotoxins (Li *et al.*, 2021). The quantities of FB1 and ZEN were significantly reduced by 56–67% and 68–75%, respectively, after the fermentation of maize meal with local LAB flora (Sangsila *et al.*, 2016). Similar to this, Franco *et al.* (2011) found that LAB successfully prevents DON and *F. graminearum* detoxification. The use of LAB as a detoxifying agent in significant agricultural crops and crop derivatives meant for human consumption is currently restricted, despite its potential.

PLANT SECONDARY METABOLITES AS A BIOCONTROL DETOXIFYING AGENT

Essential oils, spices, herbs, and crude plant extracts have a lot of potential for making bio-fungicides and nutraceuticals to treat mycotoxicosis and other infections (Bryła *et al.*, 2022;

Nazzaro *et al.*, 2017). Botanicals are often regarded as more eco-friendly and secure sources of bioagents for halting the growth of mycotoxins in food and feed (Sumalan and Poiana, 2013; Emsen *et al.*, 2016). They are also more affordable than other materials, support a synergistic defense against contamination by mycotoxins and fungi, and stimulate pathways that trigger inborn defensive systems in plant tissues. Botanicals have also demonstrated promise in enhancing the organoleptic qualities of food goods and extending their shelf life. Overall, botanicals offer a sustainable and natural alternative to conventional synthetic fungicides and preservatives, as well as a means of reducing fungal infection and the production of mycotoxin (Kalagatur *et al.*, 2018).

***Essential Oils*:** Essential oils (EOs) are organic substances that are extracted from a variety of plant parts, including roots, fruits, flowers, and seeds. They stand out due to their distinctive aroma, which is a result of the terpenes, aromatic compounds, and other secondary metabolites that plants produce (Castro *et al.*, 2020). Environmental factors like climate, rainfall, sunlight, and seasonal variations have an immediate impact on the content of the oils and their action against microbes, which in turn affects the generation of EOs and their constituents (Estrada-Cano *et al.*, 2017). EOs have been shown to stop the growth of fungi and the production of mycotoxin in a number of ways, such as changing the growth rate and lag phase of fungi, changing the permeability of cells, changing the electron transport chain, changing gene expression patterns and metabolic processes, and changing the permeability of cells (Mirza Alizadeh *et al.*, 2022). In recent years, it has become clear that a variety of EOs can inhibit both the growth of *Fusarium* and the production of mycotoxin. Cinnamon, verbena, palmarosa, orange, and spearmint, as well as Litsea cubeba, have been reported to have inhibitory effects on *Fusarium* (Gwiazdowska *et al.*, 2022). For instance, Perczak *et al.* (2019) looked at the impact of EOs from cinnamon, palmarosa, orange, and spearmint on the development of *F. graminearum* and *F. culmorum* as well as the production of mycotoxins in maize seeds. They discovered that these EOs dramatically decreased mycotoxin concentrations of ZEN (99.10–99.92%) and DON (90.69–100%) in maize seeds while also inhibiting the growth of *Fusarium* fungus. However, the effectiveness of cinnamon, verbena, and palmarosa in lowering ZEN and DON in maize grains depends on their concentration (Perczak *et al.*, 2019). Additionally, EOs containing particular constituents extracted from aromatic plants (Aloysia polystachya, Origanum vulgane, Mentha piperita, and Aloysia triphylla) inhibited fumonisin production in maize grain and the growth of *F. verticillioides* (Mani-López and López-Malo, 2021). The EOs isolated from Zingiber officinale, Cinnamomum zeylanicum, and Cymbopogon martinii were tested for their ability to inhibit the growth of *F. verticillioides* and the production of fumonisins by Castro *et al.* (2020). According to the study, all of the EOs tested had inhibitory effects on *F. verticillioides* by weakening the cell wall, shrinking the conidia, and stopping mycelial growth. The antifungal effects of *Litsea cubeba* essential oil against *F. verticillioides* were also tested separately in vitro. The results showed that mycelial growth and the production of FB1 and FB2 were greatly reduced. The EOs had a minimum inhibitory concentration of 125 g/mL, and their inhibitory activity was dose-dependent (Pante *et al.*, 2021). Additionally, the effects of temperature, pH, incubation time, mycotoxin and essential oil concentrations, as well as a number of EOs (cedarwood, cinnamon leaf, cinnamon bark, white grapefruit, pink grapefruit, lemon, eucalyptus, palmarosa, mint, thymic, and rosemary) on ZEN reduction under various in vitro conditions have also been investigated (Perczak *et al.*, 2016). In a different experiment, cinnamon oil successfully decreased FB1 from 15.03 to 0.89 g/mL (94.06%) (Xing-dong and Hua-Li, 2014). Generally, the prevention and detoxification of *Fusarium* mycotoxins found in grains are possible with the use of EOs from plants.

***Plant Extracts* (PEs):** The value of plants as a source of natural substances with a variety of health-promoting characteristics has long been acknowledged (Karataş *et al.*, 2014, 2015). They specifically contain compounds that have properties that are antimutagenic, antimicrobial, antioxidant, and anticarcinogenic, which can help lessen the damaging and genotoxic effects of mycotoxins. Numerous studies have shown that PEs are capable of preventing *Fusarium* spp. from growing and producing toxins (Ali *et al.*, 2020). The bioactive components in these extracts, such as polyphenols, phenolic acids, and flavonoids, are believed to be responsible for their antimicrobial activity. Additionally, using PEs with antimicrobial properties has become a promising strategy for reducing the need for synthetic chemicals and controlling mycotoxigenic fungi in food and feed (Makhuvele *et al.*, 2020). It has been discovered that a number of PEs exhibit antifungal effects against *Fusarium* infections. According to Garcia *et al.* (2012), extracts from Stevia rebaudiana and Equisetum arvense were successful in reducing the growth of *F. verticillioides*. Seepe *et al.* (2020) revealed that Melia azedarach acetone extract exhibited potent antifungal activity (97% inhibition) against *F. proliferatum*. Additionally, acetone extracts from Quercus acutissima and Combretum erythrophyllum combined to inhibit *F. solani*, *F. proliferatum*, and *F. verticilloides* by 96%, 67%, and 56%, respectively. According to research by Ferruz *et al.* (2016), natural phenolic acids such as caffeic, ferulic, p-coumaric, and chlorogenic can prevent *Fusarium* growth and the generation of mycotoxin in both culture medium and maize kernels. Although there has been little progress in using PEs to prevent *Fusarium* growth and mycotoxin biosynthesis in maize grains, recent studies have shown encouraging results that point to their potential use in the near future. In a study by Montibus *et al.* (2021), the effectiveness of sixteen extracts from eight different natural sources was tested against

microbial growth and the formation of type B trichothecene (TCTB) by *F. graminearum*. The extracts were prepared using subcritical water extraction at two different temperatures. The extract made from coastal pine sawdust was incredibly successful, as evidenced by the considerable suppression of up to 89% of fungal growth and a reduction of up to 65% of *F. graminearum's* mycotoxin production. Additionally, a study by Uwineza *et al.* (2022) reported that lemon balm extracts reduced mycotoxins and acted as antifungals against *F. proliferatum* and *F. culmorum*.

***Edible Mushrooms as a Source of Biological Detoxifying Agent*:** According to Savoie *et al.* (2019), edible mushrooms are macrofungi having a distinct fruiting body that can be an airborne or underground Basidiomycete or Ascomycete, large enough to be seen with the unaided eye and to be picked by hand. One of the most well-known edible mushrooms is the mushroom oyster or white-rot fungus (Pleurotus ostreatus), which has economic, ecological, and therapeutic significance (antioxidant activity and bio-compound source) (El-Ramady and Prokisch, 2021; Mihai *et al.*, 2022). The use of biocontrol organisms for mycotoxin detoxification in cereals, especially maize, has gained popularity in recent years (Branà *et al.*, 2017). This is due to the bioactive compounds such as phenolic compounds and proteins present in these organisms, as well as their highly efficient enzymatic systems such as manganese peroxide and laccases for degrading mycotoxins (Merel *et al.*, 2020; Savoie *et al.*, 2019). Furthermore, since *Fusarium*'s use as a natural detoxifying agent has been predicted for the future, other types of mushrooms have been used to inhibit the growth of the fungus and the biosynthesis of its mycotoxins. Merel *et al.* (2020) investigated the impact of crude extracts (CEs) from *A. subrufescens*, *L. edodes*, and *P. ostreatus* fruiting bodies on two strains of *F. verticillioides* that mostly contaminated maize on biomass production and mycotoxins.

***Enzymes as a Biocontrol Detoxifying Agent*:** In the past few years, a lot of work has been done to find enzymes that can effectively metabolize and break down mycotoxins. These enzymes offer a possible biotransformation solution to the problems that mycotoxicology brings up. These biotechnological approaches are characterized by their high specificity, capacity to generate non-toxic byproducts, and strong preference for achieving complete detoxification, all while adhering to eco-friendly practices (Tian *et al.*, 2022). Depending on the specific nature and type of mycotoxins, various conversion pathways have been explored, including hydrogenation, hydroxylation, oxidation, hydrolysis, esterification, glycosylation, glucuronidation, methylation, de-epoxidation, deamination, demethylation, and sulfation (Li *et al.*, 2020). Numerous encourging ideas have been published, particularly in targeting aflatoxins, fumonisins, and ochratoxins (Anukul *et al.*, 2013; Awuchi *et al.*, 2022; Gong *et al.*, 2023; Jard *et al.*, 2011; Karlovsky, 1999). The most prevalent agricultural mycotoxin DON presents significant challenges in the development of detoxifying agents due to its small polar moiety. Overcoming this obstacle has been the subject of intense research as scientists strive to discover viable and sustainable biological degradation solutions (Tian *et al.*, 2022). Through meticulous experimentation, various research teams have shed light on the mechanism of enzyme action against another prominent mycotoxin, zearalenone (ZEN), to disrupt its estrogenic activity (Jing *et al.*, 2022). The predominant mode of ZEN detoxification involves the cleavage of its lactone ring, facilitated by esterases as catalysts. This irreversible reaction influences hydroxyketones to endure decarboxylation. A novel approach utilizing a function-driven methodology combined with metagenomic analysis has emerged as a powerful tool for identifying potent enzymes involved in mycotoxin degradation (Ferrara and Gallo, 2022). Notably, Ferrara *et al.* (2022) found two new carboxylesterase genes in bacteria from the Dysgonamonadaceae and Peptococcaceae families. These genes were able to break down fumonisin, a mycotoxin of concern.

Agricultural products are frequently contaminated by multiple mycotoxins simultaneously, underscoring the importance of developing biocontrol agents that contain a combination of efficient enzymes (Lyagin and Efremenko, 2019). To address this challenge, a thorough understanding of enzyme properties and catalytic processes is crucial. It is essential to identify enzymes capable of degrading multiple mycotoxins concurrently, although only a limited number of enzymes have demonstrated such versatility. Notable examples of degradation enzymes include aldo-keto reductase AKR18A1 (causing reduction of zearalenone and trichothecenes), aflatoxin oxidase AFO (targeting sterigmatocystin and aflatoxins), and cytochromes (involved in modifying aflatoxins, sterigmatocystin, and trichothecenes) (Guan *et al.*, 2021; He *et al.*, 2017). Furthermore, it is noteworthy that certain mycotoxins, such as ergot alkaloids and sterigmatocystin, can only be effectively detoxified by a few specific enzymes, and in some cases, detoxification may not be feasible. Additionally, it is important to recognize that more than half of the known enzymes, including isomerases, translocases, lyases, and ligases, have not exhibited the capability to modify mycotoxins (Nešić and Mastanjević, 2021). Enzyme utilization offers significant advantages from both economic and technological perspectives. However, it is essential to carefully consider the potential influence of the matrix on their efficacy. The success of the detoxification process heavily relies on the physicochemical properties of the substrait, including moisture, fat content, texture, and acidity. It is important to acknowledge that the presence of masked forms of mycotoxins and inhibitory components in raw materials can hinder enzymatic catalysis (Guo *et al.*, 2020; Nešić and Mastanjević, 2021). Consequently, these factors require thorough consideration and may necessitate

pretreatments, additional financial resources, and time, particularly when implementing industrial-scale applications (Nešić and Mastanjević, 2021). The utilization of biological agents as feed preservatives may be subject to certain limitations. To ensure their commercial viability, it is crucial to understand the underlying conversion processes, assess the toxicological implications of the modified products, and evaluate their impact on the nutritional value of the feed and the overall health of the animals. It is imperative that any feed additive is both harmless and stable within the digestive tract of animals. Achieving optimal effectiveness requires the implementation of an appropriate technological approach for enzyme application that ensures its efficiency is preserved.

DISCUSSION AND FUTURE REMARKS

The *Fusarium* infection has become a significant and widespread menace in present-day agriculture, leading to substantial apprehensions over the viability of crucial crops. The aforementioned fungal infection has caused extensive devastation in multiple places, resulting in significant implications for both food security and economic stability (Anwar *et al.,* 2022; Misiou and Koutsoumanis, 2022; Pinto *et al.,* 2022). The production and distribution of mycotoxins, which are secondary metabolites produced by several fusarium species have been reported. This presents substantial health hazards to both humans and animals, as well as causing major economic losses to the agricultural and food sectors. *Fusarium*, a well-known genus of fungi, is distinguished by its capacity to generate various mycotoxins, such as zearalenones, fumonisins, trichothecenes, deoxynivalenol, nivalenol, and T-2 toxins. These mycotoxins pose a significant threat to agricultural commodities, with grains and cereals being particularly susceptible to contamination (Al-Ani, 2019; Balasubramaniyam *et al.,* 2023). The present study provides a thorough examination of current progress in the field of *Fusarium* infection research. It offers insights into the life cycle, morphological and microscopic features, molecular detection techniques, and pathogenicity variables associated with *Fusarium* infections in important agricultural crops. The results underscore the urgent necessity to immediately address this concerning situation. The adverse effects of *Fusarium* mycotoxins on agricultural commodities necessitate prompt and continuous measures to ensure the safety of the food chain and protect human health. The presence of newly identified and developing mycotoxins presents more complexities in this context, requiring novel methods of management and a proactive stance in addressing the potential threats they bring to human health (Kamle *et al.,* 2022; Mohammed *et al.,* 2022).

Biological control agents used for mycotoxin detoxification not only are effective but also economically viable for farmers. They should be formulated in a manner that ensures ease of handling and application. Enhancing their efficacy can be achieved through various strategies, including the selection of more aggressive strains of microorganisms, the combination of multiple ingredients, genetic manipulations, and the incorporation of synergistic bio-products (Abdel-Wahed and Abdel-Rahman, 2022; Ali *et al.,* 2022; Corredor-Perilla *et al.,* 2023). However, it is important to note that the biocontrol of mycotoxins should not be viewed as a standalone solution. It is crucial to integrate this approach with good agricultural practices and complement it with effective postharvest management techniques, particularly in terms of proper storage and sorting. By adopting a comprehensive approach that encompasses the entire agricultural and storage processes, we can effectively mitigate mycotoxin risks and ensure the safety and quality of agricultural products. The sustainability, safety, and ecological impact of biological strategies are paramount concerns raised by farmers, local governments, academia, and industry stakeholders. To address these concerns, rigorous evaluation and testing should be conducted to eliminate any doubts regarding adverse effects on plants and the environment. It is imperative to undertake a comprehensive risk assessment, taking into account all relevant factors, before implementing any specific method.

Also, using good agronomic and storage practices could help reduce the number of *Fusarium* infections and reduce the amount of mycotoxin contamination in both crops and processed foods (Dinolfo *et al.,* 2022; Martín *et al.,* 2022; Odjo *et al.,* 2022). The production of mycotoxins can be considerably reduced through the implementation of timely and appropriate harvesting practices, as well as optimal post-harvest handling and storage conditions. The establishment of successful solutions to address *Fusarium* infections and mycotoxin contamination necessitates the crucial involvement of researchers, policymakers, and agricultural stakeholders in collaborative efforts. It is imperative for governments to give resources and financial assistance towards research endeavors that are focused on comprehending and addressing this urgent matter. In addition, it is imperative for policymakers to implement and enforce regulatory measures aimed at facilitating the effective surveillance and control of mycotoxin concentrations in agricultural commodities and food items. Public awareness campaigns can also serve as a pivotal factor in advancing food safety and enlightening consumers of the hazards linked to *Fusarium* mycotoxins. The provision of knowledge to consumers will enable them to make well-informed decisions, thus contributing to the promotion of safe and mycotoxin-free agricultural products. In summary, the *Fusarium* infection poses a substantial and continuously escalating obstacle to contemporary agriculture and the preservation of food security. The generation of mycotoxins by *Fusarium* species presents significant hazards to both human and animal well-being, and it is imperative to acknowledge the consequential economic ramifications. Nevertheless, by means of scientific inquiry, inventive methodologies, and collaborative endeavors, we may effectively confront this pernicious

phenomenon. The process of identifying and quantifying mycotoxins, along with the implementation of effective biocontrol strategies, presents a promising opportunity to ensure food safety and safeguard public health. The involvement of diverse stakeholders, including researchers, politicians, and consumers, will play a crucial role in formulating a comprehensive and sustainable strategy to address *Fusarium* infections and reduce mycotoxin contamination. Through the use of cutting-edge technologies, the promotion of environmentally friendly farming methods, and the dissemination of knowledge to the general populace, we may effectively confront the threat presented by *Fusarium* (Bowen *et al.,* 2022; Kanwal, *et al*., 2022;Jurick 2022). In doing so, we can guarantee a more secure and improved future for both the agricultural sector and the entirety of humanity. Furthermore, the utilization of nanotechnology in the development of novel materials with the ability to selectively bind and eliminate mycotoxins from agricultural produce is increasingly gaining momentum (Javed and Cheema, 2023). In order to enhance the process of detoxification, researchers are currently investigating the application of genetic engineering techniques (Das *et al.,* 2023; Naheed *et al.*, 2023 ;Wang *et al.,* 2023;Naheed, *et al.*,2023) to cultivate crop types that possess resistance against mycotoxin contamination, ensuring the protection of our food supply.

***Conclusion*:** In conclusion, this comprehensive review sheds light on the pervasive issue of mycotoxin production by Fusarium species, providing a thorough exploration of their occurrence and diverse toxin profiles. The recent deep insight into management through biocontrol approaches marks a significant stride in mitigating the adverse effects of these toxins. Recognizing the imperative need for effective control strategies, the review underscores the importance of biocontrol methods in curbing mycotoxin contamination. The exploration of more efficient microorganism strains, genetic modifications, and synergistic combinations with other bio-products presents promising avenues for enhanced efficacy. However, acknowledging the existing challenges, achieving complete self-sufficiency in mycotoxin management remains a complex task. The synthesis of agricultural practices, postharvest strategies, and biocontrol approaches emerges as a holistic framework for mitigating mycotoxin risks. This conclusive insight calls for continued research, robust experimentation, and a collaborative effort among stakeholders to forge a resilient path toward minimizing the impact of Fusarium-induced mycotoxins on human health and agricultural productivity.

***Author's Contribution*:** All authors have an equal contribution.

Conflict of interest: There is no conflict of interest among authors.

Acknowledgment: We want to thank the anonymous reviewer for their valuable suggestions.

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